UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/498,046	02/04/2000	Sabine Neirynck	VIB-08	8244

7590 07/03/2002

James F. Haley Jr.
Fish & Neave
1251 Avenue of the Americas
New York, NY 10020-1104

EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	12

DATE MAILED: 07/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/498,046	NEIRYNCK ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-32 and 34-54* is/are pending in the application.

4a) Of the above claim(s) *42-45 and 47-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-32,34-41,46 and 52-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant amended claims 26-28, 31, 32, 38-40, 46, cancelled claim 33, and added new claims 52-54. Claims 42-45 and 47-51 remain withdrawn due to a non-election of invention. Claims 26-32, 34-41, 46, and 52-54 are under consideration. It is most appreciated that Applicant has cited support for the amendments to the claims.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Europe on August 5, 1997. It is noted, however, that applicant has not filed a certified copy of EP 97202434.3 application as required by 35 U.S.C. 119(b). Applicant has addressed this issue, but still not complied. Therefore, this notice is repeated because it still applies.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 47-49, newly presented in Amendment B have been renumbered 52-54.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-32, 34-41, 46, and 52-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The only outstanding rejection that remains from the previous Office action for claim 26, that also affects all dependent claims, is drawn to the "similar" integral membrane protein of influenza B or C virus used.

Applicant argues that one skilled in the art would recognize that the NB protein of influenza virus B and the CM2 protein of influenza virus C are "similar" integral membrane proteins to the M2 protein of influenza virus A. Applicant supports this argument with the teachings of Fields, cited in the Office action.

Applicant's arguments have been considered, but are found unpersuasive because the degree of specific "similarities" between the M2 protein and the other proteins in the other influenza viruses have not been defined in the specification and cannot be determined by the claims. Therefore, Applicant's presumption that the skilled artisan would conclude which "similar" integral membrane proteins of influenza viruses B and C are intended by the claim has no basis for support. The skilled artisan may also conclude that the only "similarity" that is required is that the proteins are expressed in the membrane, in which case there are multiple choices.

The rejection of claim 46 is maintained because the claim is still drafted in the product-by-process format.

Applicant states that the claim has been amended to obviate the rejection by requiring that the influenza virus antigen comprises the fusion protein.

Applicant's arguments and a review of the claim amendment have been considered, but are found unpersuasive because the claim does not recite the limitations Applicant has discussed. The claim is still drawn to an influenza virus antigen, which is obtained by several method steps. The antigen is not required to encode a fusion product. Therefore, the rejection is maintained for reasons of record.

Applicant's amendment to the claims raises additional issues under 35 U.S.C. 112, second paragraph.

Independent claims 26, 46, and 54 are vague and indefinite because the extracellular part of a "similar integral membrane protein of a human influenza virus B or C" cannot be determined because it is unclear what the "similar" influenza B and C proteins would be, as discussed above. In addition, it cannot be determined which "part" of the specific sequences referred to is intended. A "part" of any of the sequences could conceivably encompass one amino acid. It is presumed that this is not what Applicant intends, but because the specific "part" of any of the sequences is not clearly defined, the claims are vague and indefinite. This rejection affects all dependent claims 27-32, 34-41, 52, and 53.

Claim 54 recites the limitation "animal species" in lines 4 and 5. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-32, 34-41, 46, and 52-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection precipitated by Applicant's amendments to the claims.

The claims specify that the M2 membrane protein contains all or part of SEQ ID NOs: 1-3. There is no definition for which "part" of the sequences are required to practice the invention. As discussed above, a "part" of any of the recited sequences may encompass only one amino acid residue from any of the sequences. Given the length of each of the sequences, the scope of the genus containing any "part" of any of SEQ ID NOs: 1-3 is very broad. Further, it is noted that the claims recite "the M2 membrane protein contains all or part" (emphasis added). Therefore, the claims are not limited to portions disclosed in the individual sequences because an intact M2 protein would inherently possess all or any part of the instantly claimed sequences. Due to the lack of defining characteristics required for which "part" of the specific sequences are claimed and the broad scope encompassing every single amino acid alone or in conjunction with any number of amino acids preceding or following any single amino acid, it is determined that the disclosure does not adequately possess or describe the full genus claimed.

Claims 26-32, 34-41, and 52-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

Applicant states that amendment to claim 26 renders the rejection outlined in the first paragraph on page 6 of the Office action moot. However, for reasons discussed above, the

ambiguity in the claims have not obviated concerns outlined in the previous rejection. Therefore the rejection is maintained for reasons of record.

Applicant points to Table 1 and argues that the skilled artisan would be able to make any mutated version using recombinant techniques.

Applicant's arguments have been fully considered, but are found unpersuasive because some of the claims, specifically 36-40, recite "vaccine" which is not only a composition, but is also required to treat and prevent disease. Therefore, the "parts" of the instant SEQ ID NOs:, which have not been described are required to perform a specific function. It is maintained that the specification does not teach other possible functional fragments of M2 or the immunoprotection of the possible fragments. The specification also does not teach what would be considered a similar integral membrane protein from influenza virus B or C since these viruses do not contain M2.

Applicant asserts that polyclonal antibodies are specific.

In response, since the amended claims do not recite a limitation drawn to polyclonal antibodies, the grounds for rejection on this point are moot.

Applicant concludes that modifying the M2 domain would be routine in the art and concludes that the skilled artisan does not have to describe every single species in the disclosure.

The Examiner agrees with this assertion that every species need not be described. However, the MPEP § 2163 states that the invention must be described in sufficient detail that the skilled artisan can conclude that the inventor had possession of the claimed invention. Because the claims encompass an infinite number of possible "parts" for each of the claimed sequences and there is no generic "part" that would represent a guideline for which "part" is

crucial, it is determined that the disclosure inadequately describes the genus claimed. Moreover, it is noted in Applicant's response on page 12, that the "parts" do not just encompass the infinite number of fragments the Office is interpreting the claims to encompass, but also an infinite number of modifications to the sequences. The disclosure does not provide any guidance showing how the skilled artisan could manipulate in any way and still produce the instant invention. The "parts" and modifications to the whole or "parts" implied in the response encompass sequences with no defined structure or function. Therefore, it is maintained that the specification does not convey possession of the full genus claimed.

Applicant argues that epitopes would not be difficult to define for one skilled in the art. Applicant cites Figure 9, wherein a specific T cell epitope aided in priming mice.

Applicant's arguments have been fully considered, but it is maintained that identifying epitopes is unpredictable to one skilled in the art. It is well known in the art that even when the residues making contact with ligands are known with certainty, there is only speculation with respect to the involvement of each residue. Therefore, it is maintained that the specification does not teach how one could identify every influenza-specific T helper or cytotoxic T cell epitope.

Claims 26-32, 34-41, and 52-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Applicant reiterates that the skilled artisan would recognize what a similar protein to the influenza virus M2 protein is.

Applicant's arguments have been considered, but are found unpersuasive for reasons discussed above. The degree of specific "similarities" between the M2 protein and the other proteins in the other influenza viruses have not been defined in the specification and cannot be determined by the claims. Therefore, the skilled artisan may conclude that the only "similarity" that is required is that the proteins are expressed in the membrane, which is not limited to M2.

In response to rejections for antigenic drift/shift, the N-terminus of the M2 protein not being conserved, and immune response to the M2 protein being less durable in humans, Applicant states that the M2 protein is highly conserved within a host species and does not undergo antigenic shift/drift.

Applicant's arguments and a review of the references have been considered, but are found unpersuasive. The Fields reference is offered as evidence of antigenic shift/drift in other proteins, i.e., N and H, which sheds doubt that the instant composition would be able to protect against any strain of influenza. Applicant has convincingly demonstrated that the N-terminus of M2 proteins in the strains of Zebedee et al. are conserved among different human strains with the exception of codon 21 in two of the five human strains taught. However, due to the myriad of various human influenza viruses in existence, the limited number of strains identified by Zebedee et al., the fact that the reference teaches a residue change in almost half of the viruses studied, and the natural tendency of influenza to modify amino acids, evidenced by Fields et al., it is inconclusive whether the N-terminus of the M2 protein is truly conserved.

In response to Applicant's arguments directed against the in vitro monoclonal antibody results of Zebedee et al., this rejection is moot since the claims no longer recite the limitation.

Applicant argues that the preparation comprising the M2 protein of Slepushkin et al. was a crude cellular fraction in which the M2 protein was present in small proportions. Applicant's argues that the composition of Slepushkin is not defined and that contaminants may have influenced the outcome of the experiment. Applicant also assert that the mechanism of proteolytic activity is also undefined by the reference and concludes that the protection seen in Slepushkin et al. is different from the instant invention.

Applicant's arguments and a careful review of the reference have been considered, but are found unpersuasive. Although the preparation of Slepushkin et al. may have been crude, the instant claims recite open claim language that does not limit the contents of the compositions. Furthermore, mechanisms of protection are also not recited in the claims. Therefore, it is maintained that the concerns raised by the reference concerning the lack of durability and activity is maintained.

Applicant is convincing with respect to the working examples. This portion of the rejection is dropped. However, due to the due to the broad scope of the claims that is directed to treating and preventing any type of influenza virus infection, the unpredictable nature in the art with regard to vaccine development, the unpredictable nature of influenza viruses with regard to antigenic drift and shift, the lack of ability for the skilled artisan to make any immunoprotective fragment of the influenza M2 protein, the lack of direction provided by the inventor as to how to make or immediately identify other fragments or modified versions of the N-terminal M2 protein that are immunoprotective, the state of the art for the lack of protection developed from passive immunity in humans, the lack of working examples demonstrating that the instant antigen is protective against all types of influenza virus infection, and the state of the art indicating that the

M2 protein does not prevent initial infection, but only restricts growth in a few strains, it is determined that an undue amount of experimentation would be required of the skilled artisan to make and use the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Melnick et al. for reasons of record.

Applicant asserts that the amended claim specifies that the antigen comprises the fusion product.

A review of the amended claim has been considered, but is found unpersuasive because the claim does not require the antigen to encode a fusion product. Therefore, the rejection is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley/SAF
June 29, 2002

James C. Housel 7/1/02

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600